

## Topographic Study of Corneal Periphery in Selected Rheumatic Diseases

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### ABSTRACT

**Background:** many of autoimmune diseases associated with ophthalmological complication, such as Peripheral ulcerative keratitis.

**Objective:** to evaluate the potential changes in the peripheral corneal thickness in selected rheumatic autoimmune diseases.

**Patients and Methods:** a case control study was been held in Al-Azhar University Hospitals on 80 eyes for 40 patients and subjects. The patients and subjects was been examined by Pentacam examination.

**Results:** as regard peripheral corneal thickness, the mean peripheral thickness of RA patients was  $668.6 \pm 32.1$  micron, the mean peripheral thickness of SLE patients was  $667.5 \pm 34.8$  micron, the mean peripheral thickness of SNA patients was  $637.8 \pm 86.7$  micron and the mean peripheral thickness of control patients was  $681.2 \pm 12.8$  micron ( $p$ -value = 0.045).

**Conclusion:** the peripheral corneal thickness was thinner in autoimmune patients than in normal subjects.

**Keywords:** peripheral keratitis, autoimmune diseases, pentacam.

### INTRODUCTION

The immune system is a host defense system includes many biological structures and processes that protects against disease<sup>(1)</sup>. There are many systemic autoimmune diseases that are associated with ocular manifestation include: rheumatoid arthritis, systemic lupus erythematosus, juvenile rheumatoid arthritis and sero-negative arthritis<sup>(2)</sup>.

The common ocular manifestations of systemic autoimmune diseases include tear deficiency leading to dry eyes, or keratoconjunctivitis sicca, episcleritis, scleritis, synechiae and pupillary miosis, retinal vasculitis and peripheral ulcerative keratitis (PUK)<sup>(3)</sup>. Peripheral ulcerative keratitis (PUK) is a group of inflammatory diseases whose final common pathway is peripheral corneal thinning<sup>(4)</sup>.

Corneal topography is exceptionably useful for examining characteristics of the cornea such as shape, curvature, power and thickness<sup>(5)</sup>. Rotating Scheimpflug cameras, such as the Pentacam, is a non-invasive objective device that allows evaluation of the cornea<sup>(6)</sup>.

### AIM OF THE WORK

To evaluate the potential changes in the peripheral corneal thickness in selected rheumatic autoimmune diseases.

### PATIENTS AND METHODS

**This study was been ethically approved by al-Azhar Committee** as a case control study was been held in Al-Azhar University Hospitals. The study was carried out from December 2018 to May 2019 on 80 eyes for 40 patients and subjects to compare the peripheral corneal changes in selected rheumatic autoimmune diseases with each other and with healthy persons, by using Pentacam examination, (SIRIUS @ 3D Rotating Schimflug camera & topography system).

Rheumatic patients were taken by random sample from the Rheumatology clinics and department

in Al Azhar University Hospitals and they were matched by a control group.

**Patients and subjects were categorized into 4 groups:**

Group (1): Twenty eyes of normal subjects.

Group (2): Twenty eyes in patients with rheumatoid arthritis.

Group (3): Twenty eyes in patients with systemic lupus.

Group (4): Twenty eyes in patients with seronegative arthritis.

**Written informed consent:**

An approval of the study was obtained from Al-Azhar University academic and ethical committee. Every patient signed an informed written consent for acceptance of the operation.

**Inclusion criteria:**

- Age: 18-60 years.
- Patients with definite rheumatic autoimmune disease (Systemic lupus, rheumatoid arthritis, and seronegative arthropathy includes psoriasis, ankylosing spondylitis & juvenile rheumatoid arthritis).
- Autoimmune disease diagnosed patient at least 6 months.

**Exclusion criteria:**

- Patients with corneal opacity or scar other than that caused by rheumatic autoimmune diseases.
- Patients with glaucoma.
- Patients with history of ocular surgery.
- Patients with active uveitis.
- Contact lens users.
- Severe dry eye.
- Pregnancy.
- Any chronic use of eye drops other than tears substitutions.

**All patient and subjects were subjected to the followings:**

1. **Ophthalmological examination:** History taking, includes: name, age, gender, type of autoimmune disease period and manifestation of associated, Assessment of uncorrected and best corrected visual acuity using Snellen's chart, Measuring of IOP using Goldman applanation tonometry, Slit lamp examination for assessment peripheral corneal changes as thickness, ulceration, dryness and other abnormality, Tear film break up time. (TBUT), Binocular indirect ophthalmoscope examination and Pentacam examination, (SIRIUS @ 3D Rotating Schimflug camera & topography system).
2. **Laboratory investigation:** Complete blood picture, Erythrocyte sedimentation rate (ESR), Specific laboratory tests for each selected rheumatic autoimmune disease.

#### Statistical analysis

Data were analyzed using Statistical Program for Social Science (SPSS) version 15.0. Quantitative data were expressed as mean  $\pm$  standard deviation (SD).

Qualitative data were expressed as frequency and percentage.

The following tests were done:

- A one-way analysis of variance (ANOVA): when comparing between more than two means.
- Chi-square test: was used when comparing between non-parametric data.

Probability (P-value):

- P-value < 0.05 was considered significant.
- P-value < 0.001 was considered as highly significant.
- P-value > 0.05 was considered insignificant.
- P: statistical difference between all studied groups.
- P1: statistical difference between RA group and Control group.
- P2: statistical difference between SLE group and Control group.
- P3: statistical difference between SNA group and Control group.

## RESULTS

**Table (1): Comparison between studied groups as regard age**

Variables		RA (N = 20)	SLE (N = 20)	SNA (N = 20)	Control (N = 20)	P-value
Age (years)	Mean	54.5	43.0	30.5	37.9	< 0.001*
	$\pm$ SD	7.9	8.2	13.9	0.0	

\*: p-value < 0.001 is considered highly significant.

Table (1) shows highly statistical significant difference (**p-value < 0.001**) between studied groups as regard age. Mean age of RA patients was  $54.5 \pm 7.9$  years, Mean age of SLE patients was  $43.0 \pm 8.2$  years, Mean age of SNA patients was  $30.5 \pm 13.9$  years while it was  $37.9 \pm 5.4$  years in control group (p-value < 0.001).

**Table (2): Comparison between studied groups as regard sex**

Variables		RA (N = 20)	SLE (N = 20)	SNA (N = 20)	Control (N = 20)	P-value
Sex	Male	0 (0%)	2 (10%)	0 (0%)	2 (10%)	0.24
	Female	20 (100%)	18 (90%)	20 (100%)	18 (90%)	

Table (2) shows no statistical significant difference (p-value > 0.05) between studied groups as regard sex. There were 0 (0%) male and 20 (100%) female in RA patients, 2 (10%) male and 18 (90%) female in SLE patients, 0 (0%) male and 20 (100%) female in SNA patients while there were 2 (10%) male and 18 (90%) female in control patients, (p-value = 0.24).

**Table (3): Comparison between studied groups as regard disease duration and treatment**

Variables		RA (N = 20)	SLE (N = 20)	SNA (N = 20)	P-value
Disease duration (years)	Mean	21.1	15.2	8.0	< 0.001*
	$\pm$ SD	6.9	14.1	5.8	
Treatment	Methotrexate	6 (30%)	6 (30%)	2 (10%)	0.4
	Cortisone	9 (45%)	9 (45%)	14 (70%)	
	NSAID	5 (25%)	5 (25%)	4 (20%)	
Duration of TTT (years)	Mean	13.2	12.5	5.3	< 0.001*
	$\pm$ SD	6.7	12.0	3.8	

\*: p-value < 0.001 is considered highly significant.

Table (3) shows comparison between studied groups as regard disease duration and treatment. There was highly statistical significant difference (p-value <0.001) between studied groups as regard disease duration and treatment duration.

As regard disease duration, mean disease duration of RA patients was  $21.1 \pm 6.9$  years, mean disease duration of SLE patients was  $15.2 \pm 14.1$  years and mean disease duration of SNA patients was  $8.0 \pm 5.8$  years (p-value <0.001).

As regard treatment, there were 6 patients (30%) treated by methotrexate, 9 patients (45%) treated by cortisone and 5 patients (25%) treated by NSAID in RA group. There were 6 patients (30%) treated by methotrexate, 9 patients (45%) treated by cortisone and 5 patients (25%) treated by NSAID in SLE group. There were 2 patients (10%) treated by methotrexate, 14 patients (70%) treated by cortisone and 4 patients (20%) treated by NSAID in SNA group.

As regard treatment duration, mean treatment duration of RA patients was  $13.2 \pm 6.7$  years, mean treatment duration of SLE patients was  $12.5 \pm 12.0$  years and mean treatment duration of SNA patients was  $5.3 \pm 3.8$  years (p-value <0.001).

**Table (4): Comparison between studied groups as regard corneal thickness**

Variables		RA (N = 20)	SLE (N = 20)	SNA (N = 20)	Control (N = 21)	P-value
Central (micron)	Mean	520.4	502.3	504.8	548.5	P < 0.001*
	±SD	23.7	24.7	16.4	25.4	P1 < 0.001* P2 < 0.001* P3 < 0.001*
Peripheral (micron)	Mean	668.6	667.5	637.8	681.2	P = 0.045
	±SD	32.1	34.8	86.7	12.8	P1 = 0.42 P2 = 0.38 P3 = 0.007
C/P ratio	Mean	0.78	0.75	0.8	0.8	P = 0.083
	±SD	0.03	0.04	0.13	0.03	P1 = 0.29 P2 = 0.035 P3 = 0.86

\*: p-value < 0.001 is considered highly significant.

Table (4) shows comparison between studied groups as regard corneal thickness. There was highly statistical significant difference (p-value <0.001) between studied groups as regard central while there was no statistical significant difference (p-value >0.05) between studied groups as regard peripheral corneal thickness and also C/P ratio.

As regard central corneal thickness, the mean central thickness of RA patients was  $520.4 \pm 23.7$  micron, the mean central thickness of SLE patients was  $502.3 \pm 24.7$  micron, the mean central thickness of SNA patients was  $504.8 \pm 16.4$  micron and the mean central thickness of control patients was  $548.5 \pm 25.4$  micron (p-value < 0.001).

As regard peripheral corneal thickness, the mean peripheral thickness of RA patients was  $668.6 \pm$

32.1 micron, the mean peripheral thickness of SLE patients was  $667.5 \pm 34.8$  micron, the mean peripheral thickness of SNA patients was  $637.8 \pm 86.7$  micron and the mean peripheral thickness of control patients was  $681.2 \pm 12.8$  micron (p-value = 0.045).

As regard C/P ratio, the mean ratio of RA patients was  $0.78 \pm 0.03$ , the mean ratio of SLE patients was  $0.75 \pm 0.04$ , the mean ratio of SNA patients was  $0.8 \pm 0.13$  and the mean ratio of control patients was  $0.8 \pm 0.03$  (p-value = 0.083).

**Table (5): Comparison between studied groups as regard K (max) and K (min)**

Variables		RA (N = 20)	SLE (N = 20)	SNA (N = 20)	Control (N = 20)	P-value
K (Max) (Diopter)	Mean	44.9	47.6	45.6	43.08	< 0.001
	±SD	1.4	2.6	1.2	0.52	*
K (Min) (Diopter)	Mean	42.7	44.02	44.07	43.6	0.031
	±SD	1.4	1.9	1.5	1.6	**

\*: p-value < 0.001 is considered highly significant.

\*\*: p-value < 0.05 is considered significant.

Table (5) shows comparison between studied groups as regard K (max) & K (min). There was highly statistical significant difference (p-value < 0.001) between studied groups as regard K (max), while there is statistically significant difference (p-value < 0.05) between studied groups as regard K (min).

As regard K (max), the mean K (max) of RA patients was  $44.9 \pm 1.4$  diopter, the mean thinnest location of SLE patients was  $47.6 \pm 2.6$  diopter, the mean K (max) of SNA patients was  $45.6 \pm 1.2$  diopter and the mean K (max) of control patients was  $43.08 \pm 0.52$  diopter (p-value < 0.001).

As regard K (min), the mean K (min) of RA patients was  $42.7 \pm 1.4$  diopter, the mean K (min) of SLE patients was  $44.02 \pm 1.9$  diopter, the mean K (min) of SNA patients was  $44.07 \pm 1.5$  diopter and the mean K (min) of control patients was  $43.6 \pm 1.6$  diopter (p-value = 0.031).

## DISCUSSION

An autoimmune disease is a condition arising from abnormal immune response to a normal body parts. There are at least 80 types of autoimmune diseases. Nearly anybody can be involved<sup>(7)</sup>.

PUK has an incidence of 3 cases per million per year. There is an equal prevalence of males and females. PUK has been associated with many autoimmune disorders<sup>(8)</sup>.

Our study revealed that there was positive correlation between peripheral corneal thickness and selected autoimmune diseases (peripheral cornea was thinner in autoimmune disease patients more than non diseased persons). However, this correlation was statistically non-significant correlation.

As regard peripheral corneal thickness, the mean peripheral thickness of RA patients was  $668.6 \pm$

32.1 micron, the mean peripheral thickness of SLE patients was  $667.5 \pm 34.8$  micron, the mean peripheral thickness of SNA patients was  $637.8 \pm 86.7$  micron and the mean peripheral thickness of control patients was  $681.2 \pm 12.8$  micron (p-value = 0.045).

In **Ryu *et al.*<sup>(9)</sup>** study a total of 589 patients with RA were enrolled in this study. Among them, PUK was diagnosed in eight patients (five male, three female). Four out of six patients with PUK showed laterality. The reason that their results may have been significant while ours were not is that their study group included 589 eyes, which is much larger than our group (80 eyes).

In **Liu *et al.*<sup>(10)</sup>** study the corneal thickness was significantly thinner in patients with RA than the control group. But this study was done on patients with KCS in general and for KCS combined with autoimmune disease. Therefore, our results cannot be compared to his results.

In **Anayol *et al.*<sup>(11)</sup>** study central and thinnest corneal thickness measurements of the RA patients ( $544.43 \pm 6.79$   $\mu$ m,  $535.13 \pm 7.22$   $\mu$ m) were lower than those of the control group ( $554.54 \pm 6.25$   $\mu$ m,  $547.68 \pm 6.34$   $\mu$ m), though the difference was statistically insignificant which agreed with our study.

But In all ophthalmological criteria as IOP, visual acuity, corneal biomechanics and corneal thickness no statistical significant differences could be found, e.g. corneal thickness (RA:  $584.95 \pm 37.44$   $\mu$ m versus controls:  $571.81 \pm 38.49$ , p=0.13).

While, in **Gunes *et al.*<sup>(12)</sup>**, the CCT and PCT were thinner in RA patients compared to those in control subjects. However, there were no significant correlations between the corneal parameters and the clinical variables of RA or dry eye tests. And that may be due to using different methods in estimating peripheral corneal thickness in previous two studies. As in **Konstantopoulos *et al.*<sup>(5)</sup>** Orbscan II was used while in **Gunes *et al.*<sup>(12)</sup>**, Pentacam was used instead.

In **Yazici *et al.*<sup>(13)</sup>**, corneal changes in SLE are confined primarily to ocular surface epitheliopathy secondary to KCS, and stromal keratitis (rare), peripheral keratitis particularly marginal and segmental, which agreed with our study on peripheral corneal changes in patients with SLE.

In **Yazici *et al.*<sup>(13)</sup>**, the biomechanical properties of the cornea are altered in patients with SLE compared with normal controls. This proved that there is corneal changes associated with SLE but this study compared corneal biomechanics of the cornea as a whole. Therefore, our results - which involved peripheral cornea thickness- cannot be compared to his results.

In **Rehal *et al.*<sup>(14)</sup>**, corneal involvement in psoriasis is rare and usually secondary to the eyelid or conjunctival complications such as xerosis and trichiasis. The most common presentation is punctate epithelial keratitis, but lesions can include superficial or

deep opacities, stromal infiltrates, neovascularization, erosions, scarring, and even stromal melts.

## CONCLUSION

In this study, corneal thickness in patients with RA, SLE and seronegative arthropathy was correlated with each other and with healthy subjects. A significant positive correlation was found between peripheral corneal thinning and presence of autoimmune diseases. As the peripheral corneal thickness was thinner in autoimmune patients than in normal subjects.

## REFERENCES

- Borgelt L, O'Connell MB, Smith JA (2010):** Women's Health Across the Lifespan: A Pharmacotherapeutic Approach. Available at: <https://journals.sagepub.com/doi/abs/10.1345/aph.1P278>.
- Mehta S and Jiandani P (2007):** Ocular features of hantavirus infection. *Indian Journal of Ophthalmology*, 55(5): 378–380.
- Murray PI and Rauz S (2016):** The eye and inflammatory rheumatic diseases: the eye and rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis. *Best Practice & Research Clinical Rheumatology*, 30(5): 802–825.
- Silva BL, Cardozo JB and Marback P (2010):** Peripheral ulcerative keratitis: a serious complication of rheumatoid arthritis. *Rheumatology International*, 30(9): 1267–1268.
- Konstantopoulos A, Hossain P and Anderson DF (2007):** Recent advances in ophthalmic anterior segment imaging: a new era for ophthalmic diagnosis? *Br J Ophthalmol.*, 91:551–557.
- Piñero DP, Nieto JC and Lopez-Miguel A (2012):** Characterization of corneal structure in keratoconus. *J Cataract Refract Surg.*, 38(12):2167–83.
- Ruslan M (2007):** Recognition of microorganisms and activation of the immune response. *Nature*, 449: 819–826.
- Dana MR, Qian Y and Hamrah P (2000):** Twenty-five-year panorama of corneal immunology: emerging concepts in the immunopathogenesis of microbial keratitis, peripheral ulcerative keratitis, and corneal transplant rejection. *Cornea*, 19(5):625–43.
- Watanabe R, Ishii T, Yoshida M, Takada N, Yokokura S, Shiota Y, Fujii H, Harigae H (2015):** Ulcerative keratitis in patients with rheumatoid arthritis in the modern biologic era: a series of eight cases and literature review. *Int J Rheum Dis.*, 20(2):225–230.
- Liu Z and Pflugfelder SC (1999):** Corneal thickness is reduced in dry eye. *Cornea*, 18:403–407.
- Anayol MA, Bostancı B, Şekeroğlu MA, Şimşek M, Günaydin S, Yılmazbaş P (2017):** Assessment of Corneal Densitometry in Rheumatoid Arthritis Patients. *Turk J Ophthalmol.*, 47(3):125–129.
- Gunes A, Inal EE, Tok L, Tok O (2015):** Evaluation of central and peripheral corneal thicknesses in patients with rheumatoid arthritis. *Arq Bras Oftalmol.*, 78(4):236–40.
- Yazici AT, Kara N, Yüksel K, Altinkaynak H, Baz O *et al.* (2011):** The biomechanical properties of the cornea in patients with systemic lupus erythematosus. *Eye*, 25: 1005–1009.
- Rehal B, Modjtahedi BS, Morse LS, Schwab IR, Maibach HI (2011):** Ocular psoriasis. *J Am Acad Dermatol.*, 65: 1202–1212.